REMARKS

The Office Action dated August 26, 2003 presents the examination of claims 1, 4, 6-7, 9, 11-13, 15-18, 30-36, 40-41, and 43-44. Claims 1, 30, 32, and 36 are amended. Claim 45 is added. Support for claim 45 is found in claims 1, 4, 7, and 11. No new matter is inserted into the application.

Drawings

The Examiner states that formal drawings are required in response to the Office Action. Formal drawings are attached hereto.

Claim Objections

The Examiner maintains the objection to claims 43 and 44 for allegedly reciting "An isolated nucleic acid of claim 1…" rather than "The isolated nucleic acid of claim 1…." Applicants remind the Examiner that claims 43 and 44 were amended into independent form in the Reply after Final submitted on February 28, 2003, which was entered into the record as noted in the Advisory Action dated March 17, 2003. Thus, the objection is improper and should be withdrawn.

Rejection under 35 U.S.C. §§ 101/112, first paragraph

The Examiner rejects claims 9, 12, 13, 17, 18 and 44 under 35 U.S.C. § 101 and under 35 U.S.C. § 112, second paragraph for allegedly lacking a substantial or well-established utility. The Examiner also rejects claims 9, 12, 13, 17, 18 and 44 under 35 U.S.C. § 112, for an alleged lack of enablement. Applicants respectfully traverse. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

The Examiner relies on Peterbauer et al., *Planta* 215:839-846 (2002) to assert that raffinose synthase enzymes have a high amino acid sequence homology with seed imbibition proteins and stachyose synthases, and thusly, homology cannot be used to assert function. Applicants respectfully disagree that raffinose synthase enzymes (RFSs), seed imbibition proteins (SIPs) and stachylose synthases (STSs) cannot be distinguished from one another based upon homology.

Table 1 attached hereto shows a list of RFS, SIP, and STS proteins. Table 2 attached hereto shows the overall sequence homology (%) among the amino acid sequences of RFSs, SIPs and STSs. As shown in Table 2, homologies among RFSs, SIPs and STSs are 29-98%. However, the actual homologies between RFSs and SIPs, or RFSs and STSs are low.

For example, the homologies between RFSs and SIPs are less than 40%. Specifically, the SIP shown in Table 2 (i.e., HvSIP) has only between 29% and 39% homology with the RFSs shown in Table 2. Similarly, the homologies between RFSs and STSs are less than 45%. Specifically, the STSs shown in Table 2 (i.e., PsSTS-1, PsSTS-2, VaSTS, AmSTS, and SsSTS) all have between 35% and 44% homology with the RFSs shown in Table 2.

On the other hand, the homologies among RFSs are all 50% or higher. For example, the homology between Sc-03 and Sc-02 is 62%, the homology between Sc-04 and Sc-02 is 54%, and so on. Thus, the homologies among RFSs are higher than those homologies between RFSs and SIPs and between RFSs and STSs. As such, contrary to the Examiner's remarks, the skilled artisan could rely on homology to determine whether or not a nucleic acid would actually encode a raffinose synthase enzyme.

Moreover, RFSs, SIPs, and STPs are phylogenetically distinguishable. A molecular phylogenetic tree of the RFSs, STSs and STSs shown in Table 1 is drawn in Figure 1 attached hereto. The molecular phylogenetic tree is drawn by the UPGMA method using the gene analysis software GENETYX-SV/RC for Windows version 6.1.0 (GENETYX Corporation; http://www.sdc.co.jp/genetyx/) and using

default parameters. In the molecular phylogenetic tree, RFSs, SIPs and STSs form different groups respectively.

In summary, Table 2 and Figure 1 show that RFSs, SIPs and STSs can be easily distinguished from one another based upon a comparison of their amino acid sequences. Thus, contrary to the Examiner's remarks, amino acid sequence similarity can be used to assert function. For the above reasons, Applicants respectfully submit that the claimed invention complies with 35 U.S.C. § 101. Withdrawal of the instant rejection is therefore respectfully requested.

Further, since the claimed invention is supported by a well-established utility under 35 U.S.C. § 101, one skilled in the art would know how to use the claimed invention. Therefore, the rejection under 35 U.S.C. § 112, first paragraph is improper and should be withdrawn.

Rejection under 35 U.S.C. § 112, first paragraph, Written Description

The Examiner maintains the rejection of claims 1, 4, 7, 9, 11-13, 15-18, 30-36, 40-41, and 44 under 35 U.S.C. § 112, first paragraph for an alleged lack of written description. Applicants

respectfully traverse. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

Description based upon homology

First, the Examiner again relies on the teachings of Peterbauer et al. to assert that one of skill in the art cannot describe a raffinose synthase based upon amino acid sequence similarity. Applicants respectfully disagree for the reasons provided above. Specifically, the homologies between raffinose synthase enzymes and seed imbibition proteins or stachylose synthases are considerably lower than the homologies among raffinose synthase enzymes. Thus, one of skill in the art could describe a putative raffinose synthase based upon its sequence similarity with known raffinose synthase enzymes.

Description based upon hybridization

Second, the Examiner asserts, "[I]t is the Examiner's opinion that the description of such nucleic acid does not adequately describe other nucleic acids that hybridize to said sequences as broadly claimed in claims 1, 30, 32, and 36." From this statement, the Examiner appears to assert that the genus of nucleic acids recited in sections (i), (j), (k), and (l) of claims 1, 30, 32, and

36 are not sufficiently described in the specification. Applicants respectfully disagree.

The nucleic acids recited in sections (i), (j), (k), and (l) of claims 1, 30, 32, and 36 are described by: (1) origin of the nucleic acid, (2) the PCR primers utilized to obtain the nucleic acid, (3) the ability of the nucleic acid to hybridize with a known nucleic acid under stringent hybridization conditions, and (4) the ability of the nucleic acid to encode a protein which produces raffinose by combining a D-galactosyl group through an $\alpha(1\rightarrow6)$ bond with a hydroxyl group attached to the carbon atom at position 6 of a D-glucose residue in a sucrose molecule.

Such description is above and beyond what is required by the USPTO to meet the requirements of written description. The "Revised Interim Written Description Guidelines Training Materials" (hereinafter "the Training Materials") published by the United States Patent and Trademark Office on January 5, 2001 utilizes hybridization language to describe a genus of nucleic acids. Specifically, Example 9 of the Training Materials addresses claims that recite the invention in terms of hybridization to a reference sequence. Thus, Example 9 is relevant to the instant claims 1, 30, 32, and 36. The claim in Example 9 states:

> An isolated nucleic acid that specifically hybridizes under highly stringent conditions to the complement of the sequence set forth in SEQ ID NO: 1, wherein said nucleic acid encodes a protein that binds to a dopamine receptor and stimulates adenylate cyclase activity.

This claim language is identical in its general content to that of claims 1, 30, 32, and 36 in that both a reference sequence and a biological activity are set forth. The instant claims are even more delineated than the example provided by the USPTO in that the instant claims also limit the nucleic acids to specific origins (i.e., leguminous plant, lamiaceous plant, monocotyledon) and are obtained by the use of specific primers pairs (i.e., SEQ ID NOs: 9, 15, 55, 56, 57, or 58 and SEQ ID NOs: 10, 11, 17, or 53; SEQ ID NOs: 12, 19, 65, or 68 and SEQ ID NOs: 13, 14, 21, or 70; SEQ ID NOs: 71 or 73 and SEQ ID NOs: 72 or 74; and SEQ ID NO: 77 and SEQ ID NO:78). Claim 45 further delineates the source of the nucleic acids to broad bean, soybean, Japanese artichoke, and corn.

The disclosure in the instant specification is also above and beyond what is required by the USPTO and exemplified in Example 9. Specifically, in Example 9, there is only **one** cDNA disclosed that encodes a protein that has the biological activity recited in the claims. In contrast, the instant specification describes **a plurality** of isolated nucleic acids which encode raffinose synthase

(SEQ ID NOs: 4, 6, and 8). In any event, the USPTO considers that the disclosure of **one** species within the genus is sufficient: "Thus, a representative number of species is disclosed, since highly stringent hybridization conditions in combination with the coding function of DNA and the level of skill and knowledge in the art are adequate to determine that applicant was in possession of the claimed invention." See, Training Materials, pages 36-37. Therefore, the instant disclosure of **a plurality** of isolated nucleic acids certainly is adequate to describe the genus of nucleic acids encompassed by claims 1, 30, 32, and 36.

For all of the above reasons, Applicants respectfully submit that the pending claims are fully described in the specification such that the requirements of 35 U.S.C. § 112, first paragraph are met. Withdrawal of the instant rejection is therefore respectfully requested.

Rejection under 35 U.S.C. § 112, first paragraph, Enablement

The Examiner maintains the rejection of claims 1, 4, 7, 9, 11-13, 15-18, 30-36, 40-41, and 44 under 35 U.S.C. § 112, first paragraph for an alleged lack of enablement. Applicants respectfully traverse. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

Function based upon homology

Again, the Examiner again relies on the teachings of Peterbauer et al. to assert that one of skill in the art cannot assume the function of a raffinose synthase based upon amino acid sequence similarity. Again, Applicants respectfully disagree for the reasons provided above. Specifically, the homologies between raffinose synthase enzymes and seed imbibition proteins or stachylose synthases are considerably lower than the homologies among raffinose synthase enzymes. Thus, one of skill in the art could predict the function of a nucleic acid based upon its sequence similarity with known raffinose synthase enzymes.

Undue experimentation

The Examiner also argues that it would require undue trial and error experimentation by one of skill in the art to make and use the genus of nucleic acids claimed and confirm their function. Applicants strongly disagree.

First, the Examiner is reminded, "The fact that experimentation may be complex does not necessarily make it undue, if the art typically engages in such experimentation." U.S. Pat. & Trademark Off., *Manual Pat. Examining Proc.* § 2164.01 (8th ed. rev. 1, 2003). Second, the Examiner is reminded that the Federal Circuit has also held that a specification was enabling when "there

was considerable direction and guidance" in the specification; there was "a high level of skill in the art at the time the application was filed"; and "all of the methods needed to practice the invention were well known." In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988).

In the present case, there is a high level of skill in the art (e.g., a Ph.D. in biochemistry or its equivalent), the specification provides considerable direction and guidance (as described below), and all of the methods needed to practice the invention are known (as described below). Thus, it would not cause the skilled artisan undue experimentation to make or use the claimed nucleic acids of the present invention.

(a) Guidance in the specification

The instant specification provides PCR primers and a detailed description of how to use them to isolate additional examples of nucleic acids encoding raffinose synthase. Working examples 6-11 show the use of the PCR primers to perform such isolations. This disclosure is much more than a "mere statement that [broadly claimed DNA] is part of the invention and reference to a potential method of isolating it." Fiers v. Sugano, 25 USPQ2d 1601 (Fed. Cir. 1993). This disclosure constitutes actual variants within the claimed genus and actual methods that can be used to find the next

species within the genus. The specification further provides a detailed description of an assay that can be used to determine if the protein encoded by an isolated nucleic acid is in fact a protein which produces raffinose. Specifically, Example 2 (pages 31-32 of the specification) provides an assay for measurement of raffinose synthase activity.

(b) All of the methods needed to practice the invention are known

All of the methods need to practice the present invention are readily known by the skilled artisan. For example, section (i) of claim 1 is directed to a nucleotide sequence obtained from a polynucleotide which is amplified from a nucleic acid obtained from a leguminous plant with a combination of a PCR primer selected from the group consisting of SEQ ID NO:9, SEQ ID NO:15, SEQ ID NO:55, SEQ ID NO:56, SEQ ID NO:57, and SEQ ID NO:58 and a PCR primer selected from the group consisting of SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:17, and SEQ ID NO:53, wherein said nucleotide sequence hybridizes with a nucleotide sequence complementary to the nucleotide sequence of (a) or (b) of claim 1, in 0.9 M NaCl, 0.09 M citric acid at 65°C. Thus, the methods needed to obtain such a nucleic acid include DNA isolation from leguminous plant, PCR amplification using specific primers, and hybridization. It is uncontestable that all of these

techniques are widely utilized such that their use is routine the art.

For example, genomic libraries and PCR primers are commercially available. Automated machines can complete hundreds of PCR reactions at a time, such that the entire genus of plants could be screened within days. Thus, even if the genus of plants is large, it would not cause the skilled artisan undue experimentation to screen the genus via PCR.

In summary, considering that there is a high level of skill in the art (e.g., a Ph.D. in biochemistry or its equivalent) and that all of the methods needed to practice the invention are known and provided for in the specification (e.g., PCR and raffinose synthase activity assay), it would not be undue experimentation to make or use the claimed nucleic acids of the present invention. The instant rejection is therefore improper and should be withdrawn.

Rejection under 35 U.S.C. § 112, second paragraph

The Examiner rejects claims 1, 4, 7, 11, 15-16, and 30-36 under U.S.C. § 112, second paragraph for allegedly being indefinite. Applicants respectfully traverse. Reconsideration of the claims and withdrawal of the instant rejection are respectfully requested.

Specifically, the Examiner asserts that the phrases "obtainable," "hybridizable," and "amplifiable" in claims 1, 30, 32, and 36 are unclear. In response to the Examiner's remarks, Applicants amend these terms into past tense. These amendments are made to merely clarify idiomatic claim language and do not narrow the scope of the claims.

Applicants respectfully submit that the instant claims particularly point out and distinctly claim the subject matter that is the present invention such that the requirements of 35 U.S.C. § 112, second paragraph are met. Withdrawal of the instant rejection is therefore respectfully requested.

Provisional Double Patenting Rejection

The Examiner provisionally rejects claims 1, 4, 7, and 30-36 under the judicially created doctrine of obviousness-type double patenting for allegedly being unpatentable over claims 1, 16-22, and 28-30 of copending Application No. 09/301,766. Applicants respectfully traverse. Applicants will file a Terminal Disclaimer after either the present invention or co-pending Application 09/301,766 is allowed by the United States Patent and Trademark Office.

Allowed Claims

Claim 6 is allowed. The Examiner notes that claim 43 would be allowable if re-written into independent form. Again, Applicants remind the Examiner that claim 43 was amended into independent form in the Reply after Final submitted on February 28, 2003. Applicants respectfully request that the record be clarified to reflect this fact.

Conclusion

Applicants respectfully submit that the above remarks and/or amendments fully address and overcome the rejections of record. The present application is in condition for allowance. The Examiner is respectfully requested to issue a Notice of Allowance indicating that claims 1, 4, 6-7, 9, 11-13, 15-18, 30-36, 40-41, and 43-45 are allowed.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Kristi L. Rupert, Ph.D. (Reg. 45,702) at the telephone number of the undersigned below.

Pursuant to the provisions of 37 C.F.R. §§ 1.17 and 1.136(a), the Applicants hereby petition for an extension of three (3) months to February 11, 2004, in which to file a reply to the Office Action.

The required fee of $950.00 is enclosed herewith.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

BIRCH, STEWART, KOLASCH & BIRCH, LLP

By _____
Gerald M. Murphy, Jr., #28,977

P.O. Box 747
Falls Church, VA 22040-0747
(703) 205-8000

GMM/KLR:gmh
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Attachments: Table 1: List of RFS, SIP, and STS enzymes
Table 2: Homologies (%) among RFS, SIP, and STS enzymes
Figure 1: Phylogenetic tree of RFS, SIP, and STS enzymes
Formal drawings